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Review

Population-based Study of Septicaemia and Intestinal Infection Diseases Deaths in America and Twenty Major Developed Countries 2013-15: Indicative of Poor Food Production and Handling?

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Abstract

Introduction: American research produced evidence that USA food production and handling, and, the misuse of anti-biotics is linked to increased cases of septicaemia and food-poisoning. This led to this comparison of the extremes of this problem examining current Intestinal Infection Disease Deaths (IIDD) and Septicaemia mortality rates in the USA compared to the twenty Major Developed Countries (MDC) 2013-2015.

Methods & Material: WHO mortality data analysed for Septicaemia and IIDD mortality Age-Standardised-Deaths -Rates (ASDR) controlling for age, gender and population. In addition, Adult (55-74) and Infant (>1) death rates per million (pm) compares MDC and USA latest mortality. Odds Ratios calculated between MDC to USA to determine any substantial difference taken as >1:1.50.

Results: USA had highest Combined IDD and Sepsis. Septicaemia – USA 211pm was highest Adult rate, MDC averaged 67pm, (minus USA) yielding an MDC: USA ratio of 1:3.15, America is substantially higher than 19 MDC. USA 43pm second highest Infant, MDC averaging 17pm, a MDC: USA ratio of 1:2.53. USA is substantially higher than 17 MDC. Intestinal Disease Deaths- USA Adult joint highest at 38pm, MDC averaged 10pm, an MDC: USA ratio 1:3.80, America double 18 MDC rates. USA 59pm highest Infant, MDC averaging 6pm, a MDC: USA ratio 1:9.83, USA double all the MDC.

Conclusions: Had USA matched MDC averages there would have been 14,448 fewer American deaths. Both USA sepsis and IIDD adult and infant rates double most MDCC suggesting worse anti-biotic misuse and poor food production, perhaps indicating the WHO warning about possible future epidemic?

Keywords: intestinal infection sepsis deaths USA international

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Introduction

There has been criticism by American researchers of USA food production, food handling and medical misuse of anti-biotics, which has led to increases in cases of food-poisoning and septicaemia, which has also inadvertently led to the development of Multi-Drug-Resistant (MDR) bacteria and

micro-organisms (Hoyle 2004, Ogutta, 2008; Bonnet, 2009, Aperce 2016, Roth, 2017, Afema et al, 2017; Cummings et al, 2017; Doyle et al, 2017; Roth 2017; Gast et al, 2018; Hamilton et al, 2018.). Though this problem has also been found in other Major Developed Countries (MDC) (Folgori, 2014, Pandic, 2015; Cai 2018, Alcamo, 2019, Ballo 2019,

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Giradli, 2019, Suzuki, 2019) but it may be a greater problem in the USA?

In regard to issues of food production via animal welfare, this is related to cattle, pigs, poultry and is linked with food-poisoning in the USA (Hoyle et al, 2004; Ogutta et al, 2008; Bonnett et al, 2009; Aperce et al, 2016; Roth et al, 2017; Self et al, 2017).

Moreover, a number of USA researchers have highlighted the link with growing MDR anti-microbial resistance, evolving from poor anti-biotic use in medical treatment and, animal and avian welfare practices leading to food-born infections (Hoyle, 2004, Ogutta, 2008; Bonnet, 2009, Aperce 2016, Roth, 2017, Afema et al, 2017; Cummings et al, 2017; Doyle et al, 2017; Gast et al, 2018; Hamilton et al, 2018).

Of greater concern however is the growing link between cases of septicaemia and the development of MDR bacteria, attributed to human and animal-welfare misuse of anti-biotics, which has been noted for more than a decade (Angus, 2001, Dombrovsky, 2007, Zilberg, 2016, Barrasa-Villar, 2017, Rhee, 2017, Paoli, 2018, Giraldi, 2019). Indeed, the WHO has recently warned that the development of MDR micro-organisms is a serious threat to the foundation of modern medicine, especially surgery and should have the highest prioritisation (Rello, 2019). Furthermore, sepsis and its link with MDR bacteria has been found across a specialisms for both for child and adult patients (Thacker, 2014, Zilkberberg, 2016, Mader 2018, Alcamo, 2019; Ballo, 2019). An international study on rising septicaemia levels in low-and-middle-income countries asked whether this might also affect developed countries such as America and the UK as it reported that deaths are running into the hundreds of thousands world-wide. Indeed, in a Global Burden of Disease study,

covering 195 countries, it was noted that dialarhoea-related-deaths accounted for eighth highest cause of death for all ages and fifth for children under-five (0-4), especially infants aged <1year (Troeger et al, 2018). As would be expected, there was a marked variation between developed and developing countries and in the latter there was a range of causal pathogens, mainly rotavirus, which in Western countries are mainly related to infections acquired along the food production and processing stages, though the youngest children in all countries are at relatively higher risk (Havelaar et al, 2015; Hald et al, 2016; Food Standards Agency, 2017; Troeger et al, 2018). Other research of 95 countries, which included the USA, found that the source of intestinal infections often came from contaminated eggs, poultry and cattle due to poor animal-welfare practices (Hoyle, 2004; Bonnet 20009, Roth, 2017, Eaton et al, 2019). Whilst an American study of mortality from infectious diseases found that whilst there have been major reductions over the past twenty years, dialarhoea diseases, related to food poisoning had increased over the period (El Bacheraouil, 2018). Perhaps unexpectedly, research on salmonella infections in New York found there has been virtually no improvement over the past twenty years, which suggests a degree of complacency (Firestone & Hedberg, 2018). Crucially, the sources of such infections start very much at the beginning of the production with animal welfare (El Bacheraouli 2018; Firestone & Hedberg, 2018; Gast et al, 2018; Appling et al, 2019). This includes food-safety handling (Firestone & Hedberg, 2018; Hernandez-Patlan et, 2018; Guo et al, 2019), managing salmonella risks (Manning, 20917; Self et al, 2017; Firestone & Hedberg, 2018) and prevention of infections in different food sources, pigs, pork, shrimps, chickens etc (Painter et al, 2013; Manning,

2017; Hamilton et al, 2018; Lomonoaco, et al, 2018; Appling et al, 2019). However, there are likely to be other factors, such as life-styles and social factors patterns of disease that make people more vulnerable to infections (Painter et al, 2013; Doyle et al, 2017)? Yet as American and British research indicates most food poisonings are largely avoidable (Hald et al, 2016; FSA, 2017; Jones et al, 2017; Troeger et al, 2018).

The above studies led us to examine the extremes of cases of Sepsis and Intestinal Disease Deaths (IDD), that is mortality rates, as indicators of under-lying poor food production and handling, and misuse of anti-biotics in medicine and animal welfare to compare these mortality rates of the USA with the other twenty Major Developed Countries (MDC). As, with the exception of a comparison between Germany and the Netherlands concerning salmonella outbreaks (van Assett et al, 2017) and comparative managements of norovirus reporting in Europe (Kroneman et al, 2008), we could not find any direct comparative international research in developed countries related to intestinal infections and sepsis mortality.

The Septicaemia and IIDD and mortality rates per million (pm) population of the USA and the twenty MDC are based upon the latest available WHO data (WHO, 2020).

Sepsis and IDD rates are analysed for total rates based upon Age-Standardised-Death-Rates (ASDR) and Adults, people aged 55-74, which is below the life-expectancy of all countries under-review, and, the most vulnerable, Infants <1years (Bula-Rudas et al, 2015; Alcamo et al, 2019; Eaton et al, 2019).

There is one working null hypothesis, that there will be no substantial differences, odds ratios of $>1.1.50$ or $<1:0.50$

between USA and the other twenty Major Developed Countries sepsis and IID mortality rates.

Methods

All mortality data is drawn from the WHO (2020), updated May 2018, controlled for population, which allows comparison to be made between countries of different sizes. Total Age-Standardised-Deaths-Rates (ASDR) for IDD and Septicaemia were analysed which controls for age, gender and population. It was recognised that these rates might not be relatively to high to other mortalities. In order to gain a sense of relative seriousness, we identify any American ASDR mortality category that may be lower than the combined infectious deaths from perusing the WHO data base (2020). The main comparison was examining mortality rates for Adults aged 55-74, which is below the life-expectancy of all countries reviewed and for Infants (<1year) who are especially vulnerable (Havelaar et al, 2015; Hald et al, 2016; Food Standards Agency, 2017; Troeger et al, 2018; WHO,2020). Adult and Infant rates are determined by dividing the numbers of deaths by the age-band's population to provide a rate per million (pm) population per country. The MDC countries are Australia, Austria, Belgium, Canada, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Japan, Netherlands, New Zealand, Norway, Portugal, Spain, Sweden, Switzerland and the UK. Which it is assumed broadly shares the same medical and scientific systems though it is known that there are different configurations of the countries health care systems and expenditure on health (Harding & Pritchard 2016). Whilst deaths rates are controlled for population and age to provide a firm comparative parameter, little can be said about levels of incidence and prevalence of the disorders that does not lead to a death. So

classically, such deaths can be considered the 'tip of the iceberg'.

The rates are based on the average of the WHO latest three years 2013-2015, though four MDC earlier index years 2011-13 and 2012-14, which are indicated in the tables.

The 10th edition of the International Classification of Diseases reported in the WHO 2020, codes Septicaemia deaths as A40-A41 and sometimes reported as sepsis. Intestinal Infection Diseases Deaths are coded as A00 to A09, which includes the following. Cholera A00, typhoid & paratyphoid fevers A01, other salmonella poisonings A02, Shigellosis dysentery A03, other bacterial infections A04, other bacterial food bourn infections A05, Amoebiasis A06, other protozoal diseases A07, viral intestinal infections A08 and diarrhoea & gastroenteritis A09. We can only report deaths from the whole category but those from the developed world it would be assumed the largest single diagnostic category would be the salmonella and food bourn infections (Havelaar et al, 2015; Hald et al, 2016; FSA, 2017: Firestone & Hedberg, 2018; Appling et al, 2019).

To determine any substantial difference between the USA and each of the MDC, a series of specific MDC to USA odds ratios will be calculated for each country's two age-band mortalities and substantial differences are considered when the ratio is beyond >1:1.50.

Results

Table [1] is the current Age-Standardised-Death-Rates (ASDR) per million (pm) for IDD and Sepsis deaths. Septicaemia was higher than IDD in every country. The highest combined IDD and Sepsis rates were in the USA at 88pm, Greece 70pm and Germany 61pm, down to lows in Finland 10pm, Austria 12pm and Switzerland 16pm, averaging 30pm, minus the USA, producing a MDC: USA ratio of 1:2.93. To put these infectious disease deaths in context these USA rates were higher than the current American mortality rates for the anaemias, HIV, meningitis, pneumonia, TB., and higher than bladder, cervix, leukaemia, lymphomas, lip, melanoma, pancreas, oesophagus, ovary and stomach cancers.

Table [1] Intestinal Infections Deaths Total ASDR rates per million in USA and Major Developed Countries 2013-15. Ranked by Highest Combined ASDR.

Country & Year (2013-15)	ASDR IDD	ASDR Sepsis	ASDR Combined	2013-15 MDC:USA ratio
1. USA	17	71	88	1.00
2. Greece	1	69	70	1.26
3. Germany	22	39	61	1.44
4= Netherlands 2014-16	12	44	56	1.57
4=.Belgium	12	44	56	1.57
6. Denmark	13	32	55	1.60
7. Canada 2011-13	19	34	53	1.66

8.Portugal 2012-14	6	43	49	1.80
9. Italy	4	43	47	1.87
10. Sweden 2014-16	9	36	45	1.96
11.France 2012-14	11	30	41	2.15
12.Australia	6	34	40	2.20
13. Norway	10	29	39	2.26
14.Spain	6	27	33	2.67
15.Japan	5	26	31	2.84
16. UK	10	20	30	2.93
17. N. Zealand 2011-13	9	13	22	4.00
18.Ireland 2012-14	5	13	18	4.89
19.Switzerland	6	10	16	5.50
20=.Austria 2014-16	4	8	12	7.33
21.Finland	2	8	10	8.80

IDD and Septicaemia $\text{Rho}=+0.3706$ $p<0.05$.

Table [2] lists from highest to lowest the Adult (55-74) Septicaemia mortality rates per million (pm). Headed by the USA at 2211pm, followed by Belgium 116pm and Germany and the Netherlands 114pm down to lows of Austria 16pm, Finland 21m and New Zealand 26pm.

The MDC average was 670pm yielding a MDC : USA ratio of 1:3.15.

The USA had substantially ($>1:1.50$) higher deaths than 20 MDC and more than treble the rates of eleven other countries.

Table [3] lists the Infant (<1 year) Septicaemia deaths led by Greece 78pm then America 43pm and Italy 36pm, with seven countries having rates of less than 10pm and no sepsis deaths were recorded in Denmark and Switzerland.

The other nations average 16pm leading to a MDC to USA 1:2.69 ratio, with America having substantial higher rates than 18 other countries. Though it should be noted that compared to the other MDC Greece was the outlier, relative to the USA.

Table [4] presents Adult (55-74) IID rates, the highest being in the USA and Germany at 38pm, to the lowest in Greece at 1pm and Finland and Italy 6pm, averaging 10pm, with a MDC to USA ratio of 1:3.80 with the USA having more than treble the rates of ten other countries.

Table [2] Septicaemia Mortality Adults 55-74 rates per million USA v Major Developed Countries MDC to USA Odds Ratios. 2013-15

Country & Year (2013-15)	Adults 55-74	MDC:USA Ratio
1.USA	211	1:1.00
2. Belgium	116	1:1.83
3=.Netherlands 2014-16	114	1:1.87
3=. Germany	114	1:1.87
5.Greece	112	1:1.90
6.Sweden 2014-16	100	1:2.11
7. Italy	99	1:2.15
8. Portugal 2012-14	85	1:2.51
9. Canada 2011-13	79	1:2.70
10. France 2012-14	71	1:3.01
11. Japan	68	1:3.15
12. Australia	67	1:3.20
13. Spain	63	1:3.40
14. Denmark	56	1:3.83
15. Norway	54	1:3.98
16. Ireland 2012-14	35	1:6.16
17. UK	31	1:7.01
18.Switzerland	27	1:8.07
19. New Zealand 2011-13	26	1:8.43
20. Finland	21	1:10.0
21.Austria 2014-16	16	1:13.2
MDC Average [-USA]	67	3.15

Table [3] Septicaemia Mortality rates per million Infant (<1). USA v Major Developed Countries MDC to USA Ratios. 2013-15

Country & Year (2013-15)	<1year	MDC:USA Ratio
1.Greece	78	0.55
2.USA	43	1.00
3. Italy	36	1.19
4. Japan	34	1.33
5. New Zealand 2011-13	27	1.74
6.Sweden 2014-16	20	2.15
7. Canada 2011-13	19	2.26
8. Portugal 2012-14	15	2.87
9. UK	14	3.88
10. Germany	13	3.31
11=.Netherlands 2014-16	12	3.58
11=. Finland	12	3.73
13=. Belgium	11	3.90
13=. Australia	11	4.03
15. Spain	10	4.30
16. France 2012-14	9	4.78
17. Norway	8	5.38
18=. Ireland 2012-14	4	11.35
18=.Austria 2014-16	4	11.35
20=. Denmark	0	43.0x
20=.Switzerland	0	43.0x
MDC [-USA] Average	16	1:2.69

Table [4] Intestinal Infection Deaths (IID) 55-74+ rates per million USA v Major Developed Countries. MDC to USA Ratios

Country & Year (2013-15)	55-74 IID	MDC: USA Ratio
1=. USA	38	1:1.00
1=. Germany	38	1:1.00
3. Canada 2011-13	32	1:1.19
4=. Norway	19	1:2.00
4=. France 2012-14	19	1:2.00
6. Belgium	18	1:2.11
7=. Denmark	17	1:2.24
7=. UK	17	1:2.24
9. Netherland 2014-16	15	1:2.53
10. Portugal 2012-14	13	1:2.92
11. Sweden	12	1:3.17
12. Japan	10	1:3.80
14=. Switzerland	9	1:4.22
14=. Spain	9	1:4.22
14=. Australia	9	1:4.22
14=. Ireland 2012-14	9	1:4.22
17. New Zealand 2011-13	8	1:4.75
18=. Austria 2014-16	7	1:5.43
19=. Italy	6	1:6.33
20. Finland	2	1:19.0
21. Greece	1	1:38.8
MDC Average [-USA]	10	1:3.8

Table [5] shows IDD in infants (<1), the highest was the USA at 59pm, New Zealand 21pm and Australia and Austria 13pm. Nine countries had rates of less than 1pm, averaging 6pm, yielding a MDC to USA ratio of 1:9.82

Table [5] Infant IDD <1year rates per million in USA v Major Developed Countries. MDC to USA Ratios 2013-15.

Country & Year (2013-15)	IID <1	MDC: USA Ratio
1. USA	59	1:1.00
2. New Zealand 2011-13	21	1:2.80
3=. Australia	13	1:4.54
3=. Austria 2014-16	13	1:4.54
5. Japan	11	1:5.36
6=. Netherlands 2014-16	10	1:5.90
6=.Canada 2011-13	10	1:5.90
8. France 2012-14	8	1:7.38
10=. Germany	6	1:9.80
10=. Italy	6	1: 9.80
10=. Spain	6	1: 9.80
12. UK	5	1:11.8
14=. Norway	<1	1:59.0
14=. Sweden	<1	1:59.0
14=.Ireland	<1	1:59.0
14=.Belgium	<1	1:59.0
19=.Switzerland	0	1:59.0x
19=.Denmark	0	1:59.0x
19=.Finland	0	1:59.0x
19. Greece	0	1:59.0x
19=.Portugal 2012-14	0	1:59.0x
MDC Average (-USA)	6	1:9.83

Correlating Adult & Infant Septicaemia Rho= + 0.5091 p<0.01.

Adult IDD & Septicaemia Rho =+0.4567 p<0.025

Adult & Infant Septicaemia Rho =+0.2604 n.sig

Infant IDD & Septicaemia Rh= +0.1573 n.sig

Discussion

The main limitation to the study is that we can know anything about people with pre-existing conditions to make them more vulnerable to dying from infections. Also the IDD category covers a wide range of separate conditions, from the statistically very rare cholera in Western countries to the relatively common salmonella. Furthermore, while we do have studies reporting the numbers of infected people in the USA and the UK (Painter et al, 2013; Jones et al, 2017) we do not know the severity of their illness. Furthermore, there are different configurations of health provision amongst the countries, but this does not have appeared to influence the 'infectious disease' results as America spends by far the highest percentage of its GDP on health care (Harding & Pritchard, 2016) yet has substantially poorer results than most MDC. The one exception was Greece having the highest rate for infant sepsis mortality, which may be linked to reducing its GDP on health following the 2008 crash (Harding & Pritchard, 2016). Only country-specific research can explain individual national results.

It has been claimed that the negative media comments about American animal welfare and food standards were both inaccurate and unfair (Johnson, 2019) but these results appear to refute such a claim.

This suggests that perhaps the influence of poor food production and handling, with possible links to MDR bacteria, which can underlay sepsis, is a greater problem in the USA than most Western countries. Nonetheless, it may be thought that the highest combined death rate 88pmn in the USA, is not of serious concern yet it is higher than ten major cancer sites, so it is not insignificant.

In one sense these results are counter-intuitive when the richest and one of the most scientifically developed nations

in the world has worse infectious mortality outcomes. Consequently, we reject the null hypothesis, that there will be no substantial differences between the MDC and the USA in regard to food poisoning and sepsis deaths.

We have known for some time that infections and the development of MDR microorganism occurs via the misuse of anti-biotics in treating patients and the poor animal-welfare and food management (Hoyle et al, 2004; Ogutta et al, 2008; Jimenez-Belenguer et al, 2016; Troeger et al, 2018; Rello et al, 2019; Suzuki et al, 2019). Indeed, it is reported that there had been little change in New York salmonella over the past twenty years or increased (El Bacherouli et al, 2018; Firestone & Hedberg, 2018). It is noteworthy that most of the recent research expressing concern about animal welfare and food processing and its links to food-poisoning are mainly from the USA. Though there are growing concerns about sepsis and the growth of MDR resistant micro-organisms, linked to anti-biotic misuse in humans and animals in other developed as well as developing countries (Angus, 2001, Dombrovsky, 2007, Rhee 2017, Cia, 2018, Paoli 2018, Alcamo, 2019, Giradli, 2019, Rello, 2019).

This study sought to explore whether Sepsis and Intestinal Disease Death rates in America would be as good or better than the other major developed countries. It appears that the USA have failed that test. If the USA had matched the other nations mortality averages in 2015 there would have been 14,448 fewer American deaths. In parenthesis, in terms of incidence of food-poisoning, it was reported that there were nine million cases in the USA (Self et al, 2017) and 525,000 infections in the UK (Jones et al, 2017). Based upon their two populations this means that one in thirty-five Americans had an infection (assuming just one

person per infection) and one in more than 120 British people

Whether these results do infer a link with poor animal welfare and food production and handling, related to poorer use of anti-biotics in the USA, is still open to debate but these results provide evidence that the question is a valid one. Without wishing to be too extreme, the WHO has warned about rising MDR bacteria (Rello, 2019) and if the trend continues it could put surgery back into the 19th century and the current covid-19 pandemic should make us take seriously the increasing concern expressed by the WHO.

Whilst more country-specific and detailed research is needed, it appreciated that these results might be considered surprising, probably unwelcome. However, unless we speak truth to power, little will change, with the danger that current complacency will continue.

Declaration of Interests

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Ethics

No humans or animals were involved in the study so ethical approval was unnecessary.

Authorship

All authors contributed to the development, design of the study and to its final write-up.

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